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Welcome to STN International! Enter x:x

LOGINID: SSSPTA1626GMS

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

```
Welcome to STN International
NEWS 1
                 Web Page URLs for STN Seminar Schedule - N. America
NEWS 2
                 "Ask CAS" for self-help around the clock
NEWS 3 FEB 27
                New STN AnaVist pricing effective March 1, 2006
NEWS 4 MAY 10 CA/CAplus enhanced with 1900-1906 U.S. patent records
NEWS 5 MAY 11 KOREAPAT updates resume
NEWS 6 MAY 19 Derwent World Patents Index to be reloaded and enhanced
NEWS 7 MAY 30 IPC 8 Rolled-up Core codes added to CA/CAplus and
                 USPATFULL/USPAT2
NEWS 8
                 The F-Term thesaurus is now available in CA/CAplus
         MAY 30
NEWS
     9
        JUN 02
                 The first reclassification of IPC codes now complete in
                 INPADOC
                TULSA/TULSA2 reloaded and enhanced with new search and
NEWS 10
        JUN 26
                 and display fields
NEWS 11 JUN 28 Price changes in full-text patent databases EPFULL and PCTFULL
NEWS 12 JUl 11 CHEMSAFE reloaded and enhanced
NEWS 13 JUl 14 FSTA enhanced with Japanese patents
NEWS 14 JUl 19 Coverage of Research Disclosure reinstated in DWPI
NEWS 15 AUG 09 INSPEC enhanced with 1898-1968 archive
NEWS 16 AUG 28 ADISCTI Reloaded and Enhanced
NEWS 17 AUG 30 CA(SM)/CAplus(SM) Austrian patent law changes
NEWS 18 SEP 11
                 CA/CAplus enhanced with more pre-1907 records
NEWS 19 SEP 21
                 CA/CAplus fields enhanced with simultaneous left and right
                 truncation
                {\it CA}\left({\it SM}\right)/{\it CAplus}\left({\it SM}\right) display of {\it CA} Lexicon enhanced
NEWS 20 SEP 25
NEWS 21 SEP 25
                CAS REGISTRY(SM) no longer includes Concord 3D coordinates
NEWS 22 SEP 25
                CAS REGISTRY(SM) updated with amino acid codes for pyrrolysine
NEWS 23 SEP 28 CEABA-VTB classification code fields reloaded with new
                 classification scheme
NEWS EXPRESS
             JUNE 30 CURRENT WINDOWS VERSION IS V8.01b, CURRENT
              MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
```

AND CURRENT DISCOVER FILE IS DATED 26 JUNE 2006.

```
NEWS HOURS
              STN Operating Hours Plus Help Desk Availability
NEWS LOGIN
              Welcome Banner and News Items
NEWS IPC8
              For general information regarding STN implementation of IPC 8
NEWS X25
              X.25 communication option no longer available
```

Enter NEWS followed by the item number or name to see news on that specific topic.

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FILE 'HOME' ENTERED AT 13:25:58 ON 11 OCT 2006

Uploading

THIS COMMAND NOT AVAILABLE IN THE CURRENT FILE Do you want to switch to the Registry File? Choice (Y/n):

Switching to the Registry File...

Some commands only work in certain files. For example, the EXPAND command can only be used to look at the index in a file which has an index. Enter "HELP COMMANDS" at an arrow prompt (=>) for a list of commands which can be used in this file.

=> FILE REGISTRY

COST IN U.S. DOLLARS

SINCE FILE TOTAL ENTRY SESSION 0.21 0.21

FULL ESTIMATED COST

FILE 'REGISTRY' ENTERED AT 13:26:05 ON 11 OCT 2006
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STRUCTURE FILE UPDATES: 10 OCT 2006 HIGHEST RN 910095-75-9 DICTIONARY FILE UPDATES: 10 OCT 2006 HIGHEST RN 910095-75-9

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH June 30, 2006

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http://www.cas.org/ONLINE/UG/regprops.html

Uploading C:\Program Files\Stnexp\Queries\10566562a1.str

chain nodes :

10 11 12 13 14 15 16 18

ring nodes :

1 2 3 4 5 6 7 8 9

chain bonds :

5-11 6-16 7-15 9-10 11-12 11-13 12-14 12-18

ring bonds :

1-2 1-6 2-3 3-4 4-7 5-6 5-9 6-7 7-8 8-9

exact/norm bonds :

5-6 5-9 5-11 6-16 7-15 11-13 12-14

exact bonds :

1-2 1-6 2-3 3-4 4-7 6-7 7-8 8-9 9-10 11-12 12-18

isolated ring systems :

containing 1 :

G1:X

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:CLASS 11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 18:CLASS

Stereo Bonds:

10-9 (Single Wedge).

Stereo Chiral Centers:

9 (Parity=Don't Care)

Stereo RSS Sets:

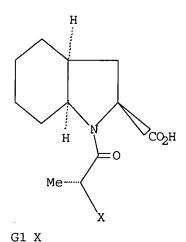
Type=Relative (Default). 1 Nodes= 9

L1 STRUCTURE UPLOADED

=> d 11

L1 HAS NO ANSWERS

L1 STI



Structure attributes must be viewed using STN Express query preparation.

=> s 11

SAMPLE SEARCH INITIATED 13:26:22 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 32 TO ITERATE

100.0% PROCESSED

32 ITERATIONS

0 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**

BATCH **COMPLETE**

PROJECTED ITERATIONS:

301 TO 979

PROJECTED ANSWERS:

0 TO

L2 0 SEA SSS SAM L1

=> s l1 sss full

FULL SEARCH INITIATED 13:26:28 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED -

586 TO ITERATE

100.0% PROCESSED

586 ITERATIONS

SEARCH TIME: 00.00.01

2 SEA SSS FUL L1

=> FIL HCAPLUS

L3

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

cool in c.b. bollend

ENTRY

SESSION 167.15

FULL ESTIMATED COST 166.94

FILE 'HCAPLUS' ENTERED AT 13:26:36 ON 11 OCT 2006 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

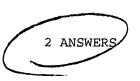
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FILE COVERS 1907 - 11 Oct 2006 VOL 145 ISS 16 FILE LAST UPDATED: 10 Oct 2006 (20061010/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s 13

L41 L3

=> d l4 ibib abs hitstr tot

ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1987:67669 HCAPLUS

DOCUMENT NUMBER:

106:67669 TITLE: Indolapril

INVENTOR (S): Linan Castellet, Isidro; Oliver Mir, Monica

PATENT ASSIGNEE(S): Farmhispania S. A., Spain; Bioiberica S. A.

SOURCE: Span., 13 pp. CODEN: SPXXAD

DOCUMENT TYPE: Patent

LANGUAGE: Spanish

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND DATE	APPLICATION NO.	DATE
ES 537841	A1 / 19860116)	ES 1984-537841	19841121
PRIORITY APPLN. INFO.:		ES 1984-537841	19841121

AB The title compound, useful as an antihypertensive (no data), was prepared An indole-2-carboxylic acid derivative was N-acylated by MeCHBrCOBr and NaHCO3 and the product was treated with (S)-PhCH2CH2CH(NH2)CO2Et and Et3N to give Indolapril.

ΙT 106534-64-9P

> RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of)

RN 106534-64-9 HCAPLUS

1H-Indole-2-carboxylic acid, 1-(2-bromo-1-oxopropyl)octahydro-, $[2S-[1(S*),2\alpha,3a\beta,7a\beta]]-(9CI)$ (CA INDEX NAME)

Absolute stereochemistry.

IT 106534-65-0P

RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of, for alkylation of aminobutyric acid derivative)

RN 106534-65-0 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-(2-bromo-1-oxopropyl)octahydro-, $[2S-[1(R^*),2\alpha,3a\beta,7a\beta]]$ - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

=> FIL REGISTRY
COST IN U.S. DOLLARS

FULL ESTIMATED COST

SINCE FILE TOTAL ENTRY SESSION 15.23 182.38

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE TOTAL ENTRY SESSION -0.75 -0.75

CA SUBSCRIBER PRICE

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New CAS Information Use Policies, enter HELP USAGETERMS for details.

10566562a1.trn

Page 6

TSCA INFORMATION NOW CURRENT THROUGH June 30, 2006

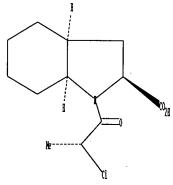
Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/reqprops.html

=>

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15 16

chain nodes :

10 11 12 13 14 15 16 18

ring nodes :

1 2 3 4 5 6 7 8 9

chain bonds :

5-11 6-16 7-15 9-10 11-12 11-13 12-14 12-18

ring bonds :

1-2 1-6 2-3 3-4 4-7 5-6 5-9 6-7 7-8 8-9

exact/norm bonds :

5-6 5-9 5-11 6-16 7-15 11-13 12-14

exact bonds :

1-2 1-6 2-3 3-4 4-7 6-7 7-8 8-9 9-10 11-12 12-18

isolated ring systems :

containing 1 :

G1:X

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:CLASS 11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 18:CLASS

Stereo Bonds:

10-9 (Single Wedge).

Stereo Chiral Centers:

9. (Parity=Don't Care)

10566562a1.trn

Page 7

Stereo RSS Sets:

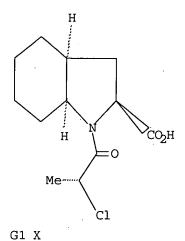
Type≈Relative (Default). 1 Nodes= 9

L5 STRUCTURE UPLOADED

=> d 15

L5 HAS NO ANSWERS

STR



Structure attributes must be viewed using STN Express query preparation.

=> s 15

SAMPLE SEARCH INITIATED 13:29:24 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED -2 TO ITERATE

100.0% PROCESSED 2 ITERATIONS

0 ANSWERS

SEARCH TIME: 00.00.01

ONLINE **COMPLETE** FULL FILE PROJECTIONS:

COMPLETE BATCH

PROJECTED ITERATIONS: 2 TO

PROJECTED ANSWERS: 0 TO

L6 0 SEA SSS SAM L5

=> s 15 sss full

FULL SEARCH INITIATED 13:29:30 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 45 TO ITERATE

100.0% PROCESSED 45 ITERATIONS 0 ANSWERS

SEARCH TIME: 00.00.01

L7 0 SEA SSS FUL L5

Uploading C:\Program Files\Stnexp\Queries\10566561a3.str

10566562a1.trn

Page 8

chain nodes : 10 11 12 13 14 15 16 19 20 21 22 29 ring nodes : 1 2 3 4 5 6 7 8 9 23 24 25 26 27 28 chain bonds : 5-11 6-16 7-15 9-10 11-12 11-13 12-14 12-19 19-20 20-21 20-22 20-26 23-29 ring bonds : 1-2 1-6 2-3 3-4 4-7 5-6 5-9 6-7 7-8 8-9 23-24 23-28 24-25 25-26 26-27 27-28 exact/norm bonds : 5-6 5-9 5-11 6-16 7-15 11-13 12-14 12-19 19-20 20-21 20-22 20-26 exact bonds : 1-2 1-6 2-3 3-4 4-7 6-7 7-8 8-9 9-10 11-12 23-29 normalized bonds : 23-24 23-28 24-25 25-26 26-27 27-28 isolated ring systems : containing 1 : 23 :

G1:X

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:CLASS 11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 19:CLASS 20:CLASS 21:CLASS 22:CLASS 23:Atom 24:Atom 25:Atom 26:Atom 27:Atom 28:Atom 29:CLASS

Stereo Bonds:

10-9 (Single Wedge).

Stereo Chiral Centers:

9 (Parity=Don't Care)

Stereo RSS Sets:

Type=Relative (Default). 1 Nodes= 9

L8 STRUCTURE UPLOADED

=> d 18

L8 HAS NO ANSWERS

L8

STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.

=> s 18

SAMPLE SEARCH INITIATED 13:33:31 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 1 TO ITERATE

100.0% PROCESSED

1 ITERATIONS

0 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**

BATCH **COMPLETE**

PROJECTED ITERATIONS:

1 TO 80

PROJECTED ANSWERS:

0 TO 0

10 0 0

0 SEA SSS SAM L8

=> s 18 sss full

FULL SEARCH INITIATED 13:33:37 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 12 TO ITERATE

0 ANSWERS

100.0% PROCESSED

SED 12 ITERATIONS

SEARCH TIME: 00.00.01

L10 0 SEA SSS FUL L8

=>

Uploading C:\Program Files\Stnexp\Queries\10566562a4.str

chain nodes :
10 11 12 13 14 15 16 19 20 21 22 23
ring nodes :
1 2 3 4 5 6 7 8 9
chain bonds :
5-11 6-16 7-15 9-10 11-12 11-13 12-14 12-19 19-20 20-21 20-22 20-23
ring bonds :
1-2 1-6 2-3 3-4 4-7 5-6 5-9 6-7 7-8 8-9
exact/norm bonds :
5-6 5-9 5-11 6-16 7-15 11-13 12-14 12-19 19-20 20-21 20-22
exact bonds :
1-2 1-6 2-3 3-4 4-7 6-7 7-8 8-9 9-10 11-12 20-23
isolated ring systems :
containing 1 :

G1:X

Match level : .

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:CLASS 11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 19:CLASS 20:CLASS 21:CLASS 22:CLASS 23:CLASS

Stereo Bonds:

10-9 (Single Wedge).

Stereo Chiral Centers:

9 (Parity=Don't Care)

Stereo RSS Sets:

Type=Relative (Default). 1 Nodes= 9

L11 STRUCTURE UPLOADED

=> d 111

10566562a1.trn

Page 11

L11 HAS NO ANSWERS L11

G1 X

Structure attributes must be viewed using STN Express query preparation.

=> s 111

SAMPLE SEARCH INITIATED 13:36:57 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 1 TO ITERATE

100.0% PROCESSED SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**

BATCH **COMPLETE**

1 ITERATIONS

PROJECTED ITERATIONS: 1 TO 80

PROJECTED ANSWERS: 0 TO 0

L12 0 SEA SSS SAM L11

=> s lll sss full

0 SEA SSS FUL L11

FULL SEARCH INITIATED 13:37:03 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 12 TO ITERATE

100.0% PROCESSED 12 ITERATIONS 0 ANSWERS

SEARCH TIME: 00.00.01

Uploading C:\Program Files\Stnexp\Queries\10566562a5.str

10566562a1.trn

L13

Page 12

13:43

0 ANSWERS

chain nodes :

10 11 12 13 14 15 16

ring nodes :

1 2 3 4 5 6 7 8 9

chain bonds :

5-11 6-16 7-15 9-10 11-12 11-13 12-14

ring bonds :

1-2 1-6 2-3 3-4 4-7 5-6 5-9 6-7 7-8 8-9

exact/norm bonds :

5-6 5-9 5-11 6-16 7-15 11-13 12-14

exact bonds :

1-2 1-6 2-3 3-4 4-7 6-7 7-8 8-9 9-10 11-12

isolated ring systems :

containing 1 :

G1:X

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:CLASS 11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS

Stereo Bonds:

10-9 (Single Wedge).

Stereo Chiral Centers:

9 (Parity=Don't Care)

Stereo RSS Sets:

Type=Relative (Default). 1 Nodes= 9

L14 STRUCTURE UPLOADED

=> d 114

L14 HAS NO ANSWERS

L14

STR

Structure attributes must be viewed using STN Express query preparation.

=> s 114

G1 X

SAMPLE SEARCH INITIATED 13:40:03 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 143 TO ITERATE

100.0% PROCESSED 143 ITERATIONS

12 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**

BATCH **COMPLETE**

PROJECTED ITERATIONS: 2143 TO 3577

PROJECTED ANSWERS: 33 TO 447

L15 12 SEA SSS SAM L14

=> s ll4 sss full

FULL SEARCH INITIATED 13:40:10 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 3181 TO ITERATE

100.0% PROCESSED 3181 ITERATIONS 243 ANSWERS

SEARCH TIME: 00.00.01

L16 243 SEA SSS FUL L14

=> FIL HCAPLUS

COST IN U.S. DOLLARS SINCE FILE TOTAL

FULL ESTIMATED COST : ENTRY SESSION 674.80 857.18

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE TOTAL

CA SUBSCRIBER PRICE ENTRY SESSION 0.00 -0.75

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FILE COVERS 1907 - 11 Oct 2006 VOL 145 ISS 16 FILE LAST UPDATED: 10 Oct 2006 (20061010/ED)

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=> d his

T₁1

L4

(FILE 'HOME' ENTERED AT 13:25:58 ON 11 OCT 2006)

FILE 'REGISTRY' ENTERED AT 13:26:05 ON 11 OCT 2006 STRUCTURE UPLOADED

L2 0 S L1

L3 2 S L1 SSS FULL

FILE 'HCAPLUS' ENTERED AT 13:26:36 ON 11 OCT 2006 1 S L3

L10 0 S L8 SSS FULL

L11 STRUCTURE UPLOADED

L12 0 S L11

L13 0 S L11 SSS FULL

L14 STRUCTURE UPLOADED

L15 12 S L14 L16 243 S L14

. 243 S L14 SSS FULL

FILE 'HCAPLUS' ENTERED AT 13:40:51 ON 11 OCT 2006

=> s 116

L17 1521 L16

L18 983 L17 AND PERINDOPRIL

=> s 118 and process

2320069 PROCESS

1574509 PROCESSES

3462426 PROCESS

(PROCESS OR PROCESSES)

L19 68 L18 AND PROCESS

=> s 119 and synthesis

1272425 SYNTHESIS

3 SYNTHESISES

67891 SYNTHESES

1 SYNTHESESES

1310499 SYNTHESIS

(SYNTHESIS OR SYNTHESISES OR SYNTHESESES)

L20 12 L19 AND SYNTHESIS

=> d 120 ibib abs hitstr tot

L20 ANSWER 1 OF 12 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

2006:796623 HCAPLUS

DOCUMENT NUMBER:

145:230528

TITLE:

Process for making highly pure

perindopril erbumine

INVENTOR(S):

Kumar, Ashok; Soudagar, Satish Rajanikant; Mathur, Arpana; Shah, Chirag Hasmukh; Gunjal, Sanjay Tukaram;

Metil, Dattatray Shamrao; Kelkar, Rahul Suresh;

Thakare, Devendra Digambar; Kumar, Bindu Manoj; Nair,

Raji

PATENT ASSIGNEE(S):

USA

SOURCE:

U.S. Pat. Appl. Publ., 6pp.

CODEN: USXXCO

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

US 2006178422 AP 20060810 US 2005-140226 20050527

PRIORITY APPLN. INFO: IN 2004-MU566 A 20040531

OTHER SOURCE(S): CASREACT 145:230528

AB A process for the synthesis and isolation of

(2S,3aS,7aS)-1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylic acid and its tert-butylamine salt, comprises the amidation of (2S,3aS,7aS)-octahydroindole-2-carboxylic acid benzyl ester and N-[(S)1-carboxybutyl]-(S)-alanine Et ester in nonreactive solvents in turn avoiding the formation of the impurity N-acetyl (2S,3aS,7aS)-octahydroindole-2-carboxylic acid benzyl ester. The de-protection of benzyl ester group is optimized by catalytic hydrogenolysis and then isolation of the product from an aqueous layer by extraction using an organic solvent, which eliminates the need for lyophilization.

This yields perindopril erbumine free of contaminants derivable from dicyclohexylcarbodiimide (e.g., dicyclohexylurea) and impurities originated by the use of Et acetate.

IT 82834-16-0P, Perindopril

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(in a process for making highly pure perindopril erbumine)

RN 82834-16-0 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

10/11/2006 109

10566562a1.trn

Absolute stereochemistry. Rotation (-).

IT 107133-36-8P, Perindopril erbumine

RL: SPN (Synthetic preparation); PREP (Preparation) (process for making highly pure perindopril erbumine)

RN 107133-36-8 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 82834-16-0 CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

CM 2

CRN 75-64-9 CMF C4 H11 N

L20 ANSWER 2 OF 12 HCAPLUS COPYRIGHT 2006 ACS on STN ACCESSION NUMBER: 2006:680403 HCAPLUS

10566562a1.trn

Page 17

DOCUMENT NUMBER:

145:124844

TITLE:

Process for the synthesis of

(2S, 3aS, 7aS) -1-(S) -alanyloctahydro-1H-indole-2-

carboxylic acid derivatives and use in the

synthesis of perindopril

INVENTOR (S):

Kumar, Ashok; Soudagar, Satish Rajanikant; Mathur, Arpana; Gunjal, Sanjay Tukaram; Panda, Nalinakshya

Balaram; Jadhav, Dilip Uttam

PATENT ASSIGNEE(S):

IPCA Laboratories Limited, India

SOURCE:

Eur. Pat. Appl., 16 pp.

CODEN: EPXXDW

DOCUMENT TYPE:

Patent English

LANGUAGE:

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO. DATE KIND APPLICATION NO. ------EP 1679072 20060712 EP 2005-113099 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, BA, HR, IS, YU

PRIORITY APPLN. INFO.:

IN 2005-MU17 A 20050106

OTHER SOURCE(S): CASREACT 145:124844

AB The invention relates perindopril [(2S,3aS,7aS)-1-[(2S)-2-[(S)-1-(2S)-2-[(S)-1-(2S)-2-(2S)-2-(2S)-1-(2S)-2-(2S)-(ethoxycarbonyl)butylamino]propionyl]octahydro-1H-indole-2-carboxylic acid] aralkyl ester salts used in the synthesis of perindopril. Thus, (2S,3aS,7aS)-octahydro-1H-indole-2-carboxylic acid was treated with N-[(S)-1-(ethoxycarbonyl)butyl]-L-alanine in CH2Cl2 in the presence of Et3N, 1-hydroxybenzotriazole, and dicyclohexylcarbodiimide to afford 99% perindopril benzyl ester. Conversion of the latter into the oxalate salt, followed by hydrogenolysis over 5% Pd/C and reaction with tert-butylamine yielded perindopril erbumine.

IT 107133-36-8P, Perindopril erbumine

> RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(process for synthesis of

alanyloctahydroindolecarboxylic acid derivs. in synthesis of perindopril)

RN 107133-36-8 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-

(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM

CRN 82834-16-0 CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

CM 2

CRN 75-64-9 CMF C4 H11 N

IT 897922-10-0P 897922-12-2P 897922-14-4P 897922-16-6P 897922-21-3P 897922-22-4P 897922-23-5P 897922-25-7P 897922-27-9P RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (process for synthesis of alanyloctahydroindolecarboxylic acid derivs. in synthesis of perindopril) RN897922-10-0 HCAPLUS CN1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, ethanedioate (9CI) (CA INDEX NAME) CM1 CRN 82834-16-0

Absolute stereochemistry. Rotation (-).

C19 H32 N2 O5

CMF

CM 2

CRN 144-62-7 CMF C2 H2 O4

RN 897922-12-2 HCAPLUS

CN Butanedioic acid, 2,3-bis[(4-methylbenzoyl)oxy]-, (2R,3R)-, compd. with (2S,3aS,7aS)-1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylic acid (9CI) (CA INDEX NAME)

CM 1

CRN 82834-16-0 CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

CM 2

CRN 32634-66-5 CMF C20 H18 O8

Absolute stereochemistry. Rotation (-).

RN 897922-14-4 HCAPLUS

CN Butanedioic acid, 2,3-dihydroxy- (2R,3R)-, compd. with (2S,3aS,7aS)-1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylic acid (9CI) (CA INDEX NAME)

CM 1

CRN 82834-16-0 CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

CM 2

CRN 87-69-4 CMF C4 H6 O6

Absolute stereochemistry.

RN 897922-16-6 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, phosphate (9CI) (CA INDEX NAME)

CM 1

CRN 82834-16-0 CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

CM 2

CRN 7664-38-2 CMF H3 O4 P

RN 897922-21-3 HCAPLUS

CN 1,2-Benzenedicarboxylic acid, compd. with (2S,3aS,7aS)-1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylic acid (9CI) (CA INDEX NAME)

CM 1

CRN 82834-16-0 CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

CM 2

CRN 88-99-3 CMF C8 H6 O4

RN 897922-22-4 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, (1S,4R)-7,7-dimethyl-2-oxobicyclo[2.2.1]heptane-1-methanesulfonate (9CI) (CA INDEX NAME)

CM 1

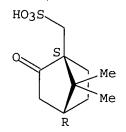
CRN 82834-16-0 CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

CM 2

CRN 3144-16-9 CMF C10 H16 O4 S

Absolute stereochemistry. Rotation (+).



RN 897922-23-5 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, 2-hydroxy-1,2,3-propanetricarboxylate (9CI) (CA INDEX NAME)

CM 1

CRN 82834-16-0 CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

CM 2

CRN 77-92-9 CMF C6 H8 O7

$$^{\mathrm{CO_2H}}_{\mid}$$
 $^{\mathrm{HO_2C-CH_2-CO_2H}}_{\mid}$ $^{\mathrm{OO_2H}}_{\mid}$ $^{\mathrm{OH}}$

RN 897922-25-7 HCAPLUS

CN Butanedioic acid, 2,3-bis[(4-methylbenzoyl)oxy]-, (2S,3S)-, compd. with (2S,3aS,7aS)-1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylic acid (9CI) (CA INDEX NAME)

CM 1

CRN 82834-16-0 CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

CM 2

CRN 32634-68-7 CMF C20 H18 O8

Absolute stereochemistry. Rotation (+).

RN 897922-27-9 HCAPLUS

CN Butanedioic acid, 2,3-bis(benzoyloxy)-, (2R,3R)-rel-, compd. with (2S,3aS,7aS)-1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-

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10/11/2006

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oxopropyl]octahydro-1H-indole-2-carboxylic acid (9CI) (CA INDEX NAME)

CM 1

CRN 82834-16-0 CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

CM 2

CRN 22333-70-6 CMF C18 H14 O8

Relative stereochemistry.

REFERENCE COUNT:

THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 3 OF 12 HCAPLUS COPYRIGHT 2006 ACS on STN

6

ACCESSION NUMBER:

2005:1262577 HCAPLUS

DOCUMENT NUMBER:

144:7098

TITLE:

Process for the preparation of

perindopril and its salts

INVENTOR(S):
PATENT ASSIGNEE(S):

Merslavic, Marjo; Smid, Janja; Tomsic, Zdenka Krka, Tovarna Zdravil D.D. Novo Mesto, Slovenia

SOURCE:

PCT Int. Appl., 19 pp.

DOCUMENT TYPE:

CODEN: PIXXD2 Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

10566562a1.trn

Page 25

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PATENT NO.
                                 DATE
                          KIND
                                              APPLICATION NO.
                                                                     DATE
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     WO 2005113500
                                 20051201
                                              WO. 2005-EP5048
                                                                      20050510
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         W: AE, AG, AL,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ,
             LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA,
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             ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
             EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,
             RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
             MR, NE, SN, TD, TG
     SI 21800
                           C
                                 20051231
                                              SI 2004-143
                                                                     20040514
     SI 21852
                           C
                                 20060228
                                              SI 2004-235
                                                                     20040805
PRIORITY APPLN. INFO.:
                                              SI 2004-143
                                                                  A 20040514
                                              SI 2004-235
                                                                     20040805
OTHER SOURCE(S):
                          CASREACT 144:7098; MARPAT 144:7098
     The invention relates to a process for the preparation of the ACE
AB
     inhibitor perindopril, its pharmaceutically-acceptable salts and
     intermediates obtained in the process. The process
     involves conversion of N-[(1S)-1-carbethoxybutyl]-L-alanine to the acid
     chloride hydrochloride and reaction with (2S,3aS,7aS)-octahydroindole-2-
     carboxylic acid or a an ester or salt. The examples describe the
     synthesis of perindopril erbumine by reactions carried
     out in CH2Cl2.
IT
     82834-16-0P, Perindopril 107133-36-8P,
     Perindopril erbumine 869954-04-1P 869954-08-5P
     869954-09-6P
     RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP
     (Preparation)
        (process for preparation of perindopril and its salts)
RN
     82834-16-0 HCAPLUS
CN
     1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-
     (ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI)
     (CA INDEX NAME)
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Absolute stereochemistry. Rotation (-).

RN 107133-36-8 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 82834-16-0 CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

CM 2

CRN 75-64-9 CMF C4 H11 N

RN 869954-04-1 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, monopotassium salt, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

● K

RN 869954-08-5 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, monolithium salt,

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(2S, 3aS, 7aS) - (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

RN 869954-09-6 HCAPLUS

1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-CN

(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, monosodium salt, (2S, 3aS, 7aS) - (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 4 OF 12 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1117891 HCAPLUS DOCUMENT NUMBER: 143:367597

TITLE: Process for the preparation of

perindopril-

INVENTOR (S): Kankan, Rajendra Narayanrao; Rao, Dharmaraj

Ramachandra

PATENT ASSIGNEE(S): Neopharma Limited, UK

SOURCE: Brit. UK Pat. Appl., 21 pp.

CODEN: BAXXDU

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT:

10566562a1.trn Page 28 13:43

PATENT INFORMATION:

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PATENT NO.
                                                   APPLICATION NO.
                             KIND
                                      DATE
                                                                              DATE
      GB 2413128
                                      2005101/9
                                                   GB 2004-8258
                                                                              20040413
                                      20051027
      WO 2005100317
                              A1
                                                   WO 2005-GB1355
                                                                              20050407
                            AM, AT, AÛ, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
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               EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,
               RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
               MR, NE, SN, TD, TG
                                                   GB 2004-8258
PRIORITY APPLN. INFO.:
                                                                          A 20040413
OTHER SOURCE(S):
                             MARPAT 143:367597
     A process for preparing perindopril or a
     pharmaceutically-acceptable salt comprises coupling a 4-halo-, 4-alkoxy-
     or 4-nitrobenzyl ester of (2S,3aS,7aS)-2-carboxyoctahydroindole with
     N-[(S)-1-carbethoxybutyl]-L-alanine (1) in the presence of DCC and HOBT,
      followed by catalytic hydrolgenolysis. The starting ester was obtained
      from (S)-indoline-2-carboxylic acid by hydrogenation-esterification and 1
     was obtained from norvaline Et ester and pyruvic acid under catalytic
     hydrogenation conditions. The method was applied to the synthesis
     perindopril erbumine (20.5 g obtained from 24 g 4-chlorobenzyl
     ester and 21.26 q 1).
IT
     82834-16-0P, Perindopril 107133-36-8P,
     Perindopril erbumine
     RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP
      (Preparation)
         (preparation of perindopril by acylation of
         octahydroindolecarboxylates with ethoxycarbonylbutylalanine)
RN
     82834-16-0 HCAPLUS
CN
     1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-
      (ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI)
      (CA INDEX NAME)
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Absolute stereochemistry. Rotation (-).

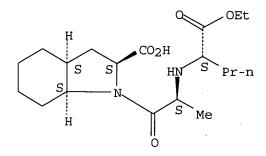
RN 107133-36-8 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 82834-16-0 CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9 CMF C4 H11 N

REFERENCE COUNT:

THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 5 OF 12 HCAPLUS COPYRIGHT 2006 ACS on STN

5

ACCESSION NUMBER:

2004:1016010 HCAPLUS

DOCUMENT NUMBER:

141:424441

TITLE:

Process for the preparation of enalapril

maleate and related compounds having ACE inhibitory

action

INVENTOR(S):

Jenko, Branko

PATENT ASSIGNEE(S): SOURCE:

Lek Pharmaceuticals D.D., Slovenia

PCT Int. Appl., 18 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

1

PATENT INFORMATION:

PATENT	NO.			KIN	D :	DATE			APPL	I CAT	ION I	NO.		D	ATE	
						ليسيمه								_		
WO 2004				A1		2004	1125		WO 2	004-	SI21			2	0040	507
W:	ΑE,	AG,	AL,	AM,	ΑT,	AU,	AZ_{μ}	ΒΆ,	BB,	BG,	BR,	BW,	BY.	BZ.	CA.	CH.
	CN,	CO,	CR,	€CU,	QZ.	-DE	DK,	DM,	DZ,	EC,	EE,	EG,	ES,	FΙ,	GB,	GD,
	GE,	GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	ΚE,	KG,	KP,	KR,	KZ,	LC,
	LK,	LR,	LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NA,	NI,

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Page 30

NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG SI 21507 С 20041231 SI 2003-123 20030516 EP 1628956 Α1 20060301 EP 2004-731808 20040507 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK PRIORITY APPLN. INFO.: SI 2003-123 A 20030516 WO 2004-SI21 20040507

OTHER SOURCE(S):

MARPAT 141:424441

The invention relates to a process for the preparation of ACE-inhibitory peptides (S,S)-R1CH2CH2CH(CO2R2)-L-Ala-NR3R4 (R1 is H, alkyl, phenyl; R2 is H, alkyl; NR3R4 is a proline, 2-piperidinecarboxylic or hexahydro-2-azepinecarboxylic acid residue and related aza/thia analogs and their esters or metal salts) in which the carboxy group of (S,S)-R1CH2CH2CH(CO2R2)-L-Ala-OH is activated with a uronium salt in an aprotic solvent prior to coupling with an amino acid HNR3R4. Thus, a mixture of N-[1(S)-(ethoxycarbonyl)-3-phenylpropyl]-L-alanine, L-proline, Et3N and O-(benzotriazol-1-yl)-N,N,N'N'-tetramethyluronium hexafluorophosphate in acetonitrile-DMF was stirred for 30 min at room temperature to afford enalapril (85.4% yield of maleate).

ΙT 87679-37-6P, Trandolapril

> RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(preparation of enalapril maleate and related compds. having ACE inhibitory action)

RN87679-37-6 HCAPLUS

CN1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)-3phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aR,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

REFERENCE COUNT:

THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

Mmy

L20 ANSWER 6 OF 12 HCAPLUS COPYRIGHT 2006 ACS on STN ACCESSION NUMBER: 2004:266899 HCAPLUS DOCUMENT NUMBER: 140:253919

3

Process for the synthesis of

W ((S)-1-(ethoxycarbonyl)butyl]-(S)-alanine for use in

the synthesis of perindopril

Breard, Fabienne; Lecouve, Jean-Pierre

10566562a1.trn

INVENTOR(S):

TITLE:

Page S 13:43

PATENT ASSIGNEE(S):

Les Laboratoires Servier, Fr.

SOURCE:

RN

CN

Eur. Pat. Appl., 9 pp.

DOCUMENT TYPE:

Patent

CODEN: EPXXDW

LANGUAGE:

French

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

	PA'	TENT	NO.			KIN	D	DATE			APPL	ICAT	ION	NO.		D.	ATE	
		1403 1403		-		Al B1		2004 2005			EP 2	003-	2924	04		2	0030	930
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	AT	2974	07			E		2005	0615		AT 2	003-	2924	04		2	0030	930
	PΤ	1403	278 ·			${f T}$		2005	0930		PT 2	003-	2924	04		2	0030	930
	ES	2240	926			Т3		2005	1016		ES 2	003-	3292	404		2	0030	930
-	WO	2005	0331	27		A1		2005	0414		WO 2	004-	FR24	63		2	0040	929
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			LK,	LR,	LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NA,	NI,
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			SN,	TD,	TG	•	•	•	•	•	- ,	,	,	- 21	,	,	,	,
PRIO	RIT	APP		-							EP 2	003-	2924	04	7	A 20	0030	930
OTHE	R SO	OURCE	(S):			MAR	PAT	140:2	2539:	19								
AB		rindo									L-Ala	HO-E	was	pre	nared	d by		
	COI	ndens	atio	n of	L-a	lanii	ne a	lkvl	or l	oenz	vl e	ster	with	n Et	alvo	xvla	ate d	or Et
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(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI)

Absolute stereochemistry. Rotation (-).

preparation of perindopril)

1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-

82834-16-0 HCAPLUS

(CA INDEX NAME)

REFERENCE COUNT:

THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS

10566562a1.trn

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

```
HCAPLUS COPYRIGHT 2006 ACS on STN
L20 ANSWER 7 OF 12
                          2004:266897 HCAPLUS
ACCESSION NUMBER:
DOCUMENT NUMBER:
                          140:253917
                          Process for the synthesis of
TITLE:
                          perindopril and its pharmaceutically-
                          acceptable salts
INVENTOR(S):
                          Dubuffet, Thierry; Langlois, Pascal
                          Les Laboratoires Servier, Fr.
PATENT ASSIGNEE(S):
                          Eur. Pat. Appl., 9 pp.
SOURCE:
                          CODEN: EPXXDW
                          Patent
DOCUMENT TYPE:
LANGUAGE:
                          French
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
     PATENT NO.
                          KIND
                           All
                                 DATE
                                              APPLICATION NO.
                                                                      DATE
                                              ------
                                                                      _____
     EP 1403275
                                 2004033/1
                                              EP 2003-290485
                                                                      20030228
                          B1 20051019
     EP 1403275
         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, EL, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK 207139 E 20051115 AT 2003-290485 20030228
     AT 307139
     ES 2250846
                           T3
                                 20060416
                                              ES 2003-3290485
                                                                      20030228
     AU 2004217599
                           A1
                                 20040916
                                           AU 2004-217599
                                                                      20040227
     WO 2004078107
                           A2
                                              WO 2004-FR446
                                 20040916
     WO 2004078107
                           A3
                                 20041021
             AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI
         RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE,
             BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU,
             MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     CN 1753906
                          A
                                 20060329
                                              CN 2004-80005405
                                                                      20040227
     JP 2006519177
                           T2
                                 20060824
                                              JP 2006-500163
                                                                      20040227
     US 2006149081
                           A1
                                 20060706
                                              US 2005-547131
                                                                      20050824
PRIORITY APPLN. INFO.:
                                              EP 2003-290485
                                                                  A 20030228
                                              WO 2004-FR446
                                                                  A 20040227
OTHER SOURCE(S):
                          MARPAT 140:253917
     A method for the synthesis of perindopril involves
     coupling of (2S)-2,3,4,5,6,7-hexahydro-1H-indolecarboxylic acid (I) or an
     ester with N-[(S)-1-carbethoxybutyl]-L-alanine, followed by catalytic
     hydrogenation. I benzyl ester tosylate was prepared by reaction of
     1-(1-cyclohexen-1-yl)pyrrolidine with (R)-ICH2CH(NBoc)CO2CH2Ph (Boc =
     tert-butoxycarbonyl), followed by deprotection and cyclization.
     Perindopril was converted into its tert-butylamine salt.
     82834-16-0P, Perindopril 107133-36-8P
ΙT
     RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP
     (Preparation)
        (synthesis of perindopril and pharmaceutically-
        acceptable salts)
RN
     82834-16-0 HCAPLUS
     1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-
CN
     (ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI)
     (CA INDEX NAME)
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10566562a1.trn

Absolute stereochemistry. Rotation (-).

RN 107133-36-8 HCAPLUS

CN lH-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 82834-16-0 CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

CM 2

CRN 75-64-9 CMF C4 H11 N

REFERENCE COUNT:

3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 8 OF 12 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

2004:247009 HCAPLUS

DOCUMENT NUMBER:

140:253916

TITLE:

Process for the synthesis of

10566562a1.trn

Page 34

```
N-[(S)-1-(ethoxycarbonyl)butyl]-(S)-alanine for use in
                            preparation of perindopril
INVENTOR(S):
                            Breard, Fabienne; Lecouve, Jean-Pierre
PATENT ASSIGNEE(S):
                            Les Laboratoires Servier, Fr.
SOURCE:
                            Eur. Pat. Appl., 9 pp.
                            CODEN: EPXXDW
DOCUMENT TYPE:
                            Patent
LANGUAGE:
                            French
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
     PATENT NO.
                                    DATE
                            KIND
                                                 APPLICATION NO.
                                                                          DATE
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                                                 -----
     EP 1400531
                                    20040324
                                                 EP 2003-292405
                                                                          20030930
                            B1 🔼
     EP 1400531
                                   20060104
          R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
              IE, SI, LT
                            LV EL RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
     AT 315046
                             E
                                   20060215
                                              AT 2003-292405
     ES 2256693
                             Т3
                                   20060716
                                                 ES 2003-3292405
                                                                          20030930
     WO 2005033128
                             Α1
                                   20050414
                                                WO 2004-FR2464
                                                                          20040929
              AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
              CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
              GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
              LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
              NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
         TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
              SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE,
              SN, TD, TG
PRIORITY APPLN. INFO.:
                                                 EP 2003-292405
                                                                       A 20030930
OTHER SOURCE(S):
                           MARPAT 140:253916
     (S)-EtO2CCHPr-L-Ala-OH was prepared by a multistep procedure starting with
     allylation of Et glyoxylate with allylzinc bromide. Subsequent steps were
     resolution using Pseudomonas Fluorescens lipase, triflation of
      (R)-EtO2CCH(OH)CH2CH:CH2, substitution reaction with benzyl L-alaninate,
     and catalytic hydrogenolysis.
ΙT
     82834-16-0P, Perindopril
     RL: PNU (Preparation, unclassified); PREP (Preparation)
         (process for synthesis of (carbethoxybutyl)-L-
        alanine in preparation of perindopril)
     82834-16-0 HCAPLUS
RN
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Absolute stereochemistry. Rotation (-).

(CA INDEX NAME)

CN

1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-

(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI)

REFERENCE COUNT:

THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 9 OF 12 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

2003:947713 HCAPLUS

DOCUMENT NUMBER:

139:381760

TITLE:

Method for synthesis of perindopril

and its pharmaceutically acceptable salts Dubuffet, Thierry; Lecouve, Jean-Pierre

INVENTOR(S): PATENT ASSIGNEE(S):

Les Laboratoires Servier, Fr.

Eur. Pat. Appl., 8 pp.

SOURCE:

CODEN: EPXXDW

DOCUMENT TYPE:

Patent

LANGUAGE:

French

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT	NO.		KIN	D DATE			APPL	ICAT	ION	NO.		D	ATE	
EP 1367 EP 1367	 061 061		A1 B1	2003	1203 0104	-			 2916			2	0030	630
R:	AT, BE,	CH,	DE,	DK, ES,	FR,	GB,	GR,	IT,	LI,	LU,	NL,	SE,	MC,	PT,
AT 3150				FI, RO,										c 2 0
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	253721													
	003153													
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				LU, LV,										
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RW:	BW, GH,	GM,	KΕ,	LS, MW,	MZ,	NA,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,
				MD, RU,										
	EE, ES,													
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m. 1000	SN, TD,		_											
CN 1802.			A											
	178421		A1	2006	0810								0051	
PRIORITY APP	LN. INFO	.:					EP 20						0030	
OMITED GOIDAE	(0)		a. a.				WO 2					W 2	0040	528
OTHER SOURCE	(5):		CASI	REACT 13	9:38:	1760	; MAI	RPAT	139	:381	760			

pharmaceutically-acceptable salts (e.g., the tert-butylamine) involves cyclocondensation reaction of N-[(S)-1-carbethoxybutyl]-(S)-alanine with

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AΒ

A method for the synthesis of perindopril and its

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sulfinyl chlorides R1SOCl (R1 = imidazolyl, benimidazolyl, or tetrazolyl) to give Et (2S)-2-[(4S)-4-methyl-2,5-dioxo-1,2,3-oxathiazolidin-3yl]pentanoate, which is amidated with (2S)-2,3,4,5,6,7-hexahydro-1H-indole-2-carboxylic acid and hydrogenated over 10% Pt/C to give perindopril. 82834-16-0P, Perindopril 107133-36-8P IT RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation) (synthesis of perindopril via cyclocondensation of carbethoxybutylalanine with imidazolesulfinyl chloride) RN 82834-16-0 HCAPLUS CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

RN 107133-36-8 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM . 1

CRN 82834-16-0 CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

CM 2

CRN 75-64-9 CMF C4 H11 N

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NH2
H3C-C-CH3
     CH3
```

THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS

2

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 10 OF 12 HCAPLUS COPYRIGHT 2006 ACS on STN 2003:910218 HCAPLUS

ACCESSION NUMBER: DOCUMENT NUMBER:

REFERENCE COUNT:

139:365227

INVENTOR(S):

TITLE:

SOURCE:

New process for the synthesis of

N-[(S)-1-earboxybutyl]-(S)-alanine esters and their

use in the synthesis of perindopril Breard, Fabienne, Fugier, Claude

Les Laboratoires Servier, Fr.

Eur. Pat. Appl., 5 pp. CODEN EPXXDW

DOCUMENT TYPE:

LANGUAGE:

Patent French

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT ASSIGNEE(S):

PA'	TENT	NO.			KIN	D	DATE				I CAT	-			D	ATE	
	1362 1362				A2 A3	_	2003 2004	1119 0331			003-				2	00309	901
	R:	AT, IE,			DE,	DK,	ES,	FR, MK,	GB,								PT,
	2004	2704	32		A1		2005	0317	i	AU 2	004-	2704	32	,	20	00408	
	2536 2005				AA A1		2005	0317 0317	Ţ	WO 2	004 - 2 004 - 2	2536 FR22	926 13		20)0408)0408	331 331
		ΑE,	AG,	AL,	AM,	AT,	ΑU,		BA,	BB,	BG,	BR,	BW,	BY,	ΒZ,	CA,	CH,
		GE,	GH,	GM,	HR,	HU,	ID,	ΙL,	IN,	IS,	JP,	ΚE,	KG,	KP,	KR,	ΚZ,	LC,
		LK, NO,	LR, NZ,	LS, OM,	LT, PG,	LU, PH,	LV, PL.	MA, PT,	MD, RO.	MG, RU.	MK, SC.	MN, SD.	MW, SE.	MX, SG.	MZ, SK	NA, SL	NI, SY
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CD T	1025	SN,	TD,	TG													
	1835				A			0920			004-8						
	2006				А		2006	0310									
PRIORITY	(APP	LN.	LNFO	. :							003-2 004-1				A 20 V 20	00309 00408	
OTHER SOURCE(S):						CASREACT 139:365227: MARPAT 139:365227											

CASREACT 139:365227; MARPAT 139:365227

Title alanine derivs. (S)-RO2CCHPr-L-Ala-OH (R = C1-C6 alkyl) were prepared from N-protected (S)-5-methyl-2-morpholinone by propylation or allylation/hydrogenation, ring opening by LiOH, esterification, oxidation of the hydroxy group, and deprotection. In an example, N-[(S)-1carbethoxybutyl]-(S)-alanine hydrochloride was prepared via allylation of Boc-protected (S)-5-methyl-2-morpholinone and treatment of tert-Bu (3S,5S)-5-methyl-3-propyl-2-oxo-4-morpholinecarboxylate with LiOH in aqueous MeCN and then EtI to afford intermediate Et (2S)-2-[(tertbutoxycarbonyl) [(1S)-2-hydroxy-1-methylethyl]amino]pentanoate.

IT 82834-16-0P, Perindopril

RL: PNU (Preparation, unclassified); PREP (Preparation) (process for synthesis of N-[(S)-carboxybutyl]-L-alanine esters for use in synthesis of perindopril)

RN 82834-16-0 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

L20 ANSWER 11 OF 12 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

2003:609507 HCAPLUS

DOCUMENT NUMBER:

139:149930

TITLE:

Process for the preparation of high purity

perindopril and intermediates useful in its

synthesis

INVENTOR(S):

Simig, Gyula; Mezei, Tibor; Porcs-Makkay, Marta;

Mandi, Attila

PATENT ASSIGNEE(S):

Les Laboratoires Servier, Fr.

SOURCE:

Eur. Pat. Appl., 12 pp. CODEN: EPXXDW

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND DATE	APPLICATION NO.	DATE
EP 1333026 R: AT, BE, CH, IE, SI, LT,	A1 20030806, DE, DK, ES, FK, LV, FI, BØ, MK,	EP 2002-290206 GB, GR, IT, LI, LU, NL, CY, AL, TR	
CA 2474003	AA 20030807	CA 2003-2474003	20030129
WO 2003064388		WO 2003-IB691	20030129
WO 2003064388	A3 20040205		
W: AE, AG, AL,	AM, AT, AU, AZ,	BA, BB, BG, BR, BY, BZ,	CA, CH, CN,
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		JP, KE, KG, KP, KR, KZ,	
		MK, MN, MW, MX, MZ, NO,	
		SG, SK, SL, TJ, TM, TN,	
	UZ, VC, VN, YU,		
RW: GH, GM, KE,	LS, MW, MZ, SD,	SL, SZ, TZ, UG, ZM, ZW,	AM, AZ, BY,
KG, KZ, MD,	RU, TJ, TM, AT,	BE, BG, CH, CY, CZ, DE,	DK, EE, ES,
		LU, MC, NL, PT, SE, SI,	
		GQ, GW, ML, MR, NE, SN,	

EE 200400107	A.	20041015	EE	2004-107		20030129
BR 2003007293	Α	20041221	BR	2003-7293		20030129
CN 1622936	Α	20050601	CN	2003-802714		20030129
US 2005119492	A1	20050602	US	2003-503272		20030129
JP 2005521667	T2	20050721	JP	2003-564011		20030129
NO 2004003472	Α	20040820	NO	2004-3472		20040820
BG 108858	Α	20050531	BG	2004-108858		20040827
PRIORITY APPLN. INFO.:			ΕP	2002-290206	Α	20020130
			WO	2003-IB691	W	20030129

OTHER SOURCE(S):

MARPAT 139:149930

The invention relates to 1-[2(S)-[1(S)-(ethoxycarbonyl)butylamino]propiony l]-(3aS,7aS)octahydroindole-2(S)-carboxylic acid (perindopril) and its tert-butylamine salt, free of contaminants derivable from dicyclohexylcarbodiimide, and a process for their synthesis. The invention also relates to N-[1-(ethoxycarbonyl)butyl]-N-(alkoxycarbonyl)alanine intermediates used in the synthesis of perindopril, a known ACE inhibitor. Thus, N-[1-(ethoxycarbonyl)butyl]-N-(ethoxycarbonyl)alanine, prepared by ethoxycarbonylation of N-[1-(ethoxycarbonyl)butyl]alanine, was treated with thionyl chloride in CH2Cl2 and acylated by perhydroindole-2-carboxylic acid in THF at reflux for 4-4.5 h. The product was treated with tert-butylamine to afford 55% perindopril eburmine.

IT 82834-16-0P, Perindopril 107133-36-8P,

Perindopril ebumine

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(process for preparation of high purity perindopril and intermediates useful in its synthesis)

RN 82834-16-0 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

RN 107133-36-8 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 82834-16-0 CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

CM 2

CRN 75-64-9 CMF C4 H11 N

REFERENCE COUNT:

THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 12 OF 12 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

2002:641139 HCAPLUS

DOCUMENT NUMBER:

138:142607

TITLE:

On-line simultaneous determination of S- and R-

perindopril using amperometric biosensors as

detectors in flow systems

AUTHOR (S):

Stefan, Raluca-Ioana; van Staden, Jacobus F.; Mulaudzi, Ludwig Vusimuzi; Aboul-Enein, Hassan Y.

CORPORATE SOURCE:

Department of Chemistry, University of Pretoria,

Pretoria, 0002, S. Afr.

SOURCE:

Analytica Chimica Acta (2002), 467(1-2), 189-195

CODEN: ACACAM; ISSN: 0003-2670

PUBLISHER:

Elsevier Science B.V.

DOCUMENT TYPE: LANGUAGE: Journal English

AB Two types of flow systems were selected for the simultaneous assay of S-and R-perindopril (pdp): flow injection anal. (FIA) and sequential injection anal. (SIA). The SIA system was more efficient, because of the highest precision and accuracy, and the lower consumption of sample and buffer. The amperometric biosensors used as detectors in the flow systems were based on 1- and d-amino acid oxidase (AAOD). The linear concentration ranges are in the nmol 1-1 range, from 120 pmol 1-1 to 40 nmol 1-1 (3+S.D.), with very low detection limits. The biosensors/flow system can be used reliably online in synthesis process control, for the simultaneous assay of S- and R-pdp with a

frequency of more than 30 samples per h.

82834-16-0, Perindopril 145513-48-0 RL: ANT (Analyte); ANST (Analytical study).

(resolution of perindopril using amperometric biosensors as detectors in flow systems)

IT

RN 82834-16-0 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

RN 145513-48-0 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2R)-2-[[(1R)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2R,3aR,7aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

REFERENCE COUNT:

22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> log y COST IN U.S. DOLLARS SINCE FILE TOTAL ENTRY SESSION FULL ESTIMATED COST 73.97 931.15 DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE TOTAL ENTRY SESSION CA SUBSCRIBER PRICE -9.00 -9.75

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